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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/941,438	08/28/2001	Dale P. DeVore	50063/018002	6389

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EXAMINER
NAFF, DAVID M

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/941438	DeVore et al
Examiner	**Group Art Unit**
Mark	1657

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 8/28/01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 1-36 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☒ Claim(s) 1-36 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☐ Information Disclosur Statement(s), PTO-1449, Paper No(s)._____

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing R vi w, PTO-948

☐ Interview Summary, PTO-413

☐ Notic of Informal Patent Application, PTO-152

☐ Other_____

Office Action Summary

Claims examined on the merits are 1-36 which are all claims in the application.

Specification

The disclosure is objected to because of the following informalities: the specification is unclear at page 6, line 6 as to whether 37° is degrees F or degrees C.

Appropriate correction is required.

Claim Objections

Applicant is advised that should claim 26 be found allowable, claim 32 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The only difference in the claims is that the preamble of claim 32 requires an implant whereas the preamble of claim 26 requires a composition. The composition is inherently an implant and the implant is inherently a composition.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9-19, 21-24 and 26-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for tissue that is decellularized and is acylated with a ratio of acylating agent to wet tissue weight of about 0.001:1 to about 0.003:1, does not reasonably provide enablement for acylating tissue that is not decellularized as in claims 33-36, and acylating with a ratio of acylating agent to tissue that encompasses any amount of acylating agent less than 0.3% as in claims 1-7, 9-19, 21-24 and 26-36. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification describes only acylating tissue that is decellularized tissue, and using a ratio of acylating agent as set forth above. Acylating tissue that is not decellularized with a ratio of acylating agent other than as set forth above is not described and enabled. Any amount of acylating agent below 0.3%, i.e. less than a ratio of 0.003:1, would not be operable since very low amounts of acylating agent would not sufficiently disperse the tissue, and presence of the acylating agent would not make a significant difference.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In step c of claim 1, and where recited in other claims, "ratio of said acylating agent to wet tissue weight is about 0.003:1 or less" is confusing as to meaning and scope. Does this set a maximum or minimum level on the amount of acylating agent present? It is suggested that the amount of acylating agent be set forth in terms of percent as described in the specification (page 11, lines 22-26) by reciting "0.3% or less". If a lower limit is recited as suggested above, then the range should be "0.1% to 0.3%".

In claims 8, 20 and 25, reciting a range of "about 0.002:1 to about 0.001:1" where the range has a lower limit of amount of acylating agent recited after an upper limit of the amount of acylating agent is confusing. The lower limit of the range should be before the upper limit of the range.

In claim 3 and where required in other claims, "cryomilling" is uncertain as to meaning and scope. The steps that constitute cryomilling should be set forth.

Claim 21 and claims dependent thereon are confusing and unclear by claim 21 failing to set forth clear, distinct and positive process steps in the order in which they are carried out. The meaning of "altering the condition of *in situ* tissue" and "effective amount of a dispersed collagen matrix being at the site of the *in situ* tissue" is unclear. Does this mean that *in situ* tissue is tissue of a subject and the

dispersed collagen matrix is implanted in the subject? If this is the case, the claim should require implanting the dispersed collagen matrix in a subject to alter tissue of the subject.

Claims 28-31 and 33-36 are confusing as to how the collagen matrix is resistant to trypsin. To be clear, it is suggested that trypsin resistance be required in the claims as defined in the specification at page 6, lines 4-6. For example, in claim 28, line 2, before "greater" insert -- such that --, and after "40%" insert -- of the dispersed collagen matrix remains undigested when exposed to 2% trypsin at 37^0 for 6-24 hours --. This same type of change should be made to other claims that require trypsin resistance. It is uncertain as to whether the 37 is degrees F or degrees C, and the appropriate degrees should be inserted in the above recitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Kelman et al (5,332,802).

The claims are drawn to an injectable composition containing an acylated, dispersed, dermal tissue matrix having a resistance to trypsin

greater than about 40%, greater than 50%, greater than 70% or greater than 90%.

Kelman et al disclose an injectable composition (col 10, lines 55-56, and col 16, lines 53-55) containing dispersed dermal tissue (col 15, lines 9-48) that has been prepared by removing an epidermal layer, cryopulverizing the resultant dermal tissue (col 15, lines 21, 23 and 31), and treating the tissue with succinic anhydride (col 15, line 54) as an acylating agent (col 7, line 44) to solubilize collagen of the tissue.

The dermal tissue in the composition of Kelman et al inherently has a trypsin resistance of greater than 90% as presently claimed. It is noted that the specification discloses (page 14, lines 10-20, page 15, Table 1 and page 19, Table 4) that lower amounts (about 0.16-0.20%) of acylating agent provides greater trypsin resistance. However, these results appear to be obtained when using glutaric anhydride as the acylating agent. It has not been established that the same results will be obtained when using all acylating agents within the scope of the claims. When using succinic anhydride as disclosed Kelman et al, trypsin resistance as claimed may be obtained at a higher concentration of acylating agent such as 0.5%. Additionally, Kelman et al pulverize frozen dermal tissue (col 15, lines 10-35) which is cryomilling, and the present specification discloses (page 14, lines 27-28) that cryomilling alone produces significant improvements in resistance to trypsin.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-36 art rejected under 35 U.S.C. 103(a) as being unpatentable over Kelman et al.

The claims require contacting decellularized dermal or connective tissue with an acylating agent to provide a ratio of acylating agent to wet tissue weight of about 0.003:1 or less and/or to provide a trypsin resistance as described above.

Kelman et al is described above.

When carrying out the process of Kelman et al of treating tissue with an acylating agent, it would have required only limited routine experimentation and been obvious to select a preferred optimum amount of acylating agent to use for a particular acylating agent. Treatment of tissue as disclosed by Kelman et al (col 15, lines 10-48) will inherently decellularize the tissue. Kelman et al is using an amount of acylating agent to totally disperse and solubilize the collagen content of the

tissue (col 7, lines 50-54). When less than total dispersion and solubility is sufficient, it would have been obvious to use lower amounts of the acylating agent. Moreover, there is inadequate evidence to establish that using about 0.3% provides results significantly different than when using 0.5% acylating agent as disclosed by Kelman et al. It should be noted that "about 0.3%" encompasses an amount of acylating agent higher than 0.3%. As to trypsin resistance, the comments set forth above apply. Using tissue other than dermal tissue such as connective tissue for treating with an acylating agent as disclosed by Kelman et al would have been a matter of individual preference depending on the function of a particular tissue desired.

Claims 1-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abraham et al (5,993,844) or Livesey et al (5,336,6160 or Goldstein (5,899,936) in view of Kelman et al.

The invention is described above.

Abraham et al (col 4, lines 55-60), Livesey et al (col 5, lines 1-16) and Goldstein ((col 5, lines 15-50) disclose producing decellularized tissue for implanting.

Kelman et al is described above.

It would have been obvious to treat the decellularized tissue of Abraham et al, Livesey et al or Goldstein with an acylating agent as suggested by Kelman et al to solubilize collagen of the tissue. It would have been further obvious to carry out cryopulverization of the tissue to facilitate acylating and to obtain an injectable composition as further suggested by Kelman et al. The comments set forth above in regard to

amount of acylating agent, trypsin resistance and the type of tissue also apply to this rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is (703) 308-0520. The examiner can normally be reached on Monday-Thursday and every other Friday from about 8:30 AM to about 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, a message can be left on voice mail.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn, can be reached at telephone number (703) 308-4743.

The fax phone number is (703) 872-9306 before final rejection or (703) 872-9307 after final rejection.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 1657

DMN
11/5/02